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LETTER TO THE EDITOR

Possible shunt infection with *Ureaplasma urealyticum* in an ELBW preterm

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Dear Editor:

This letter reports a case of an unusual causative agent of shunt infections. CSF shunt infections contribute to a tremendous burden of morbidity. Hydrocephalic children, in particular preterms, are known to be prone to shunt infections, with an infection rate up to 22%, immediate diagnosis and therapy is mandatory. The most causative pathogens are *Staphylococci spp.* but unusual pathogens also occur in this particular group of shunt patients. In a certain number of shunt infections, a causative agent could not be found. [2] *Ureaplasma spp.* and *Mycoplasma spp.* are frequent commensals, with low virulence, and regularly do not lead to invasive disease. [1] Preterms and newborns, however, are at risk to inflammatory responses due to these pathogens. *Ureaplasma spp.*, in particular, are well known to cause meningitis and hydrocephalus following inflammation of the CNS, with a high prevalence in very low- and extremely low-birth-weight preterm infants (VLBW and ELBW). [5] We report on a boy giving us a lesson to learn about unusual shunt infections.

A male ELBW infant had been born at 23 + 3 weeks of gestation with a birth weight of 450 g. He underwent an extremely complex postnatal period, with pulmonary haemorrhage, severe respiratory distress syndrome, intraventricular haemorrhage Grade III and necrotizing enterocolitis. He was finally implanted with a VP shunt when he had been 6-month-old. After shunt insertion, he had made a good recovery. At the age of 7 months, he was admitted for vomiting and a bulging fontanel. An occluded peritoneal tube was diagnosed and revised. Routinely obtained CSF samples were unremarkable, and no pathogens were detectable in routine microbial cultures. The postoperative course was uneventful, and the infant was discharged 5 days after surgery.

Three months later at the age of 10 months, the boy was readmitted due to vomiting. Ventricle size was unchanged, with no evidence of CSF shunt dysfunction. Blood sampling was unremarkable, despite 18,000 leukocytes/μl. CRP was negative with no fever, but CSF samples showed significant pleocytosis (117 leukocytes/μl with 80% lymphocytes, protein level of 182 mg/dl, glucose level of 11 mg/dl and lactate 3.0 mmol/l), indicative of CSF shunt infection. The VP shunt was removed, and an external ventricular drainage was inserted. An antibiotic regimen with ampicillin and cefotaxime was initiated. Microbial examinations of the VP shunt and repetitive CSF samples revealed no causative pathogen. CSF pleocytosis persisted despite multiple changes of empiric antibiotic regimen. An intrathecal course of vancomycin for 5 days also had no effect on the CSF findings. Finally, *Ureaplasma urealyticum* was detected from CSF samples by PCR. The infant was started on erythromycin. But inflammatory CSF parameters only improved gradually, so the external ventricular drainage was changed. After that, CSF parameters normalised subsequently. After 10 days, CSF cultures and PCR showed negative results for *Ureaplasma*, and a VP shunt was reinserted.

During a follow-up of 3 years, no further adverse events occurred. Neurological development of the boy was better than expected. He was lively, able to walk without assistance, spoke single words and interacted intensely with others. In a considerable amount of shunt infections, no causative pathogen could be detected (9 to 36%). But in most of these cases, empiric antibiotic regimens were able to cure these infections. [2] But in some cases, inflammation of CSF persisted despite extensive diagnostics and therapy.

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Ureaplasma implies special diagnostic difficulties because of complex nutritional requirements and their fastidious nature. Special media for *Ureaplasma* specimens is warranted. These pathogens are not detectable on Gram staining because of a lack of cell walls. [5] Most of the *Ureaplasma* isolates are able to form biofilms in vitro that contribute to their antibiotic resistance and ability to evade host immune responses [4] and may contribute to the capacity for causing shunt infections. Furthermore, it is able to persist in mucosal tissue in both children and adults [4]. This may serve as a possible reservoir for occasional infections triggered by shunt revisions for instance. We cannot entirely exclude the possibility that detection of *Ureaplasma* is a residual of a previous infection as appropriate diagnostics in the early preterm period are lacking. However, the success of target-specific therapy and the following non-detection of *Ureaplasma* is highly indicative for *Ureaplasma* being the causative agent of shunt infection in this case.

Ureaplasma diagnosis is not covered by routine microbiological examination. Hence, the search for *Ureaplasma* needs to be initiated by the clinician in suspicious circumstances. Furthermore, standard antibiotic regimens fail to eradicate *Ureaplasma* because macrolides are recommended for antibiotic treatment in the case of invasive disease with *Ureaplasma*. [3] But due to their toxicity, macrolides are not the first choice for infants, unless *Ureaplasma* is isolated from CSF.

The possibility of a CSF shunt infection with *Ureaplasma* should be taken into account when microbial diagnostics are unable to reveal a causative agent, and CSF inflammation persists despite of adequate antibiotic treatment. Especially in cases of VLBW and ELBW preterms, the suspicion of invasive disease with *Ureaplasma* should be raised and appropriate microbial diagnostics such as PCR and special specimen culture should be initiated.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with animals performed by any of the authors.

Statement of informed consent Informed consent was obtained from all individual participants included in the study.

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